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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/687,122	10/13/2000	Alessandra Boe	P/717-181(CONT)	6984

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EXAMINER
MURPHY, JOSEPH F

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 08/13/2002 11

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/687,122	BOE ET AL.	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

-- The MAILING DATE of this c mmunication appears on the cover sheet with the correspondence address --

Period f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 July 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-29* is/are pending in the application.

4a) Of the above claim(s) *18-20 and 22-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21 and 25-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of group II, and the elected species TBP-1 in Paper No. 10, 7/24/2002 is acknowledged. The traversal is on the ground(s) that the fact that the proteins differ with respect to their structure is insufficient to justify the requirement. This is not found persuasive because the inventions are distinct as noted in the last Office Action, as shown by the distinctness described therein and a search is directed to references which would render the invention obvious, as well as references directed to anticipation of the invention, and therefore requires a search of relevant literature in many different areas of subject matter.

Claims 18-20, 24 are withdrawn from consideration pursuant to 37 CFR 1.142(b). Claims 21 and 25-29 are under consideration.

The requirement is still deemed proper and is therefore made FINAL.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 21, 25-29 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3-4, 5 of U.S. Patent No. 6,225,300 (Boe et al.) in view of U.S. Patent No. 5,691,320 (von Borstel et al.).

Claims 1, 3-4, 5 of the '300 patent are drawn to treatment of bacterial infections and septic shock. The '320 patent discloses that Sepsis (or in its more severe form, septic shock), is one example of a broader class of disease called the "Systemic Inflammatory Response Syndrome" (SIRS), which is an organism's reaction to inflammatory stimuli such as endotoxin (which can be present in the bloodstream without bacteremia, e.g. due to leakage of endotoxin from gram-negative bacteria into the circulation from a localized infection or from the intestine) and that SIRS can also be triggered by gram-positive bacteria. Thus, it would have been obvious to one of skill in the art at the time the invention was made to practice a method of treating inflammation with TNF receptor or TBP-1 in combination with DHEA. The motivation is provided in the '320 patent which discloses the nexus between bacterial infection and inflammation (column 1, lines 36-43).

Specification

The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

On page 1, lines 31-32 of the instant Specification, Applicant's attempt to incorporate by reference the subject matter of a cited foreign application or patent (i.e. EP 0308378, 398,327 and 433,900) which sets forth the sequence of the TNF Inhibitory protein. However, this document encompasses essential matter, and the sequence of the TNF Inhibitory protein is essential for the method for treating autoimmune and inflammatory diseases in a patient which comprises administration of r-h-TBP-1 in combination with DHEA. Therefore, the above cited documents encompass essential subject matter, which cannot be incorporated by reference to patents or applications published by foreign countries or a regional patent office (See MPEP 608.01(p)). Clearly, the amino acid sequence of the TNF Inhibitory Protein is necessary for practicing a method for treating autoimmune and inflammatory diseases in a patient which comprises administration of r-h-TBP-1 in combination with DHEA

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21, 25-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating autoimmune and inflammatory diseases in a patient which comprises administration of r-h-TBP-1 in combination with DHEA, does not reasonably provide enablement for a method for treating autoimmune and inflammatory diseases in a patient which comprises administration of any functional derivatives of TNF receptor or TBP-1 in combination with DHEA. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claims 21, 25-29 are overly broad in the recitation of "TNF receptor" and "TBP-1 since insufficient guidance is provided as to which of the myriad of polypeptide species encompassed by the claims will retain the characteristics of TNF receptor or TBP-1and function in the claimed method. The terms TNF receptor and TBP-1 encompass functional derivatives of the TNF Inhibitory protein (see EP 0308378 page 11, line 40). Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible derivatives of TNF receptor or TBP-1. It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. For example, Voet et al.

(1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

Since the terms TNF receptor and TBP-1 encompasses functional derivatives (see EP 0308378 page 11, line 40), and given the art recognized unpredictability of the effect of mutations on protein function, it would require undue experimentation to practice the claimed method. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors considered to be relevant in the instant case are set forth below:

(1) the breadth of the claims - The claims are drawn to a method for treating autoimmune and inflammatory diseases in a patient which comprises administration of any functional derivatives of TNF receptor or TBP-1 in combination with DHEA

(2) the nature of the invention - The instant invention is a method for treating autoimmune and inflammatory diseases in a patient which comprises administration of any functional derivatives of TNF receptor or TBP-1 in combination with DHEA.

(3) the state of the prior art - The Voet reference demonstrates that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function.

(5) the level of predictability in the art - The Voet reference demonstrates the unpredictability of the protein art.

(6) the amount of direction provided by the inventor - Applicant has only taught methods using TNF receptor, not derivatives of TNF receptor.

(7) the existence of working examples - Working examples are provided only for one r-h-TBP-1, not derivatives of TNF receptor or TBP-1.

(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. Given the breadth of claims 21, 25-29 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to practice the claimed invention.

Claims 21, 25-29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

These are genus claims. The terms TNF receptor and TBP-1 encompass functional derivatives of the TNF Inhibitory protein (see EP 0308378 page 11, line 40). The specification and claims do not indicate what distinguishing attributes shared by the members of the genus.

The specification and claim do not place any limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to TNF receptor of TBP-1. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Although the specification states that these types of changes are routinely done in the art, the specification and claim do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, r-h-TBP-1 alone is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21, 25-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 21, 25-29 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: There is no result step set forth in the claim.

Conclusion

No claim is allowed.

DAVID S. ROMEO
PRIMARY EXAMINER

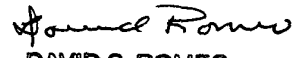
Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
August 6, 2002



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